Date of NADA Approval: OCT 51998

# FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 41-061

## MECADOX® 10 Type A Medicated Article
## (carbadox)

"... for the establishment of a 42-day slaughter withdrawal period."

Sponsored by:
Pfizer Animal Health

## I. GENERAL INFORMATION

| | |
|---|---|
| NADA Number: | 41-061 |
| Sponsor: | Pfizer Animal Health<br>812 Springdale Drive<br>Exton, Pennsylvania 19341-2803 |
| Established Name: | carbadox |
| Trade Name: | MECADOX® 10 Type A Medicated Article |
| Marketing Status: | Over-the-counter (OTC) |
| Effect of Supplement: | This supplement provides for the establishment of a 42-day slaughter withdrawal period for carbadox in swine tissues. |

## II. INDICATIONS FOR USE

MECADOX® 10 is indicated for the control of dysentery and bacterial enteritis and for growth promotion in swine.

## III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND RECOMMENDED DOSAGE

A. Dosage Form: MECADOX® 10 is a Type A Medicated Article used in the preparation of Type B and Type C medicated feeds.

B. Route of Administration: MECADOX® 10 is administered orally in finished feed.

C. Recommended Dosage: MECADOX® 10 is administered *ad libitum* in a final feed at a concentration of 10, 25, or 50 grams per ton.

## Iv. EFFECTIVENESS

Studies demonstrating the efficacy of carbadox for the control of dysentery and bacterial enteritis and for growth promotion are documented in the Freedom of Information (FOI) Summary for the original approval for MECADOX® 10 under NADA 41-061.

## V. ANIMAL SAFETY

Studies demonstrating the safety of carbadox for use in swine is contained in the FOI Summary for the original approval for MECADOX® 10 under NADA 41-061.

## VI. HUMAN SAFETY

A. Toxicity Studies: As documented in the Freedom of Information (FOI) Summary for NADA41 -061 dated January 30, 1998.

B. Safe Concentrations of Total Residues: As documented in the FOI Summary for NADA 41-061 dated January 30, 1998.

C. Total Residue and Metabolism Studies: As documented in the FOI Summary for NADA 41-061 dated January 30, 1998.

D. Determination of the tolerance for the marker residue: As documented in the FOI Summary dated January 30, 1998, FDA selected liver as the target tissue and quinoxaline-2-carboxylic acid (QCA) as the marker residue. FDA determined that when QCA (marker residue) is at or below 30 ppb in the liver (target tissue) no residue of carcinogenic concern is detectable in each of the edible tissues by any method.

E. Determination of the Withdrawal Time: Study Number 2522A-60-97-077

1. Purpose: A tissue residue study was conducted to determine the depletion profile of quinoxaline-2-carboxylic acid (QCA) residue in uncooked porcine liver and muscle tissue following oral administration (via the feed) of carbadox (MECADOX® 10) for 28 days at 55 ppm (50 grams per ton) to growing swine.

2. Investigators: This study was conducted in two phases.

| Phase one (live phase): | Phase two (analytical phase): |
|---|---|
| Martha Ferris, D.V.M., M.S.<br>Colorado Animal Research Enterprises, Inc.<br>Fort Collins, CO 80524 | Dr. Joe Boison<br>Government of Canada<br>Canadian Food Inspection Agency<br>Centre for Veterinary Drug Residues<br>Saskatoon, SK |

3. Animals: Thirty-four crossbred pigs (17 gilts and 17 barrows)

4. Dosage form: Feed containing 55 ppm carbadox.

5. Pertinent parameters measured: Muscle and liver were collected from each animal for QCA residue analysis. All of the tissue samples were analyzed in triplicate. For the purpose of establishing a withdrawal period only the liver residues were used.

6. Results: See Table 1.

**Table 1.** Arithmetic means (±SD) for quinoxaline-2-carboxylic acid (in ppb) in uncooked liver and muscle tissue of growing swine fed carbadox at 55 ppm for 28 days

| | | | QCA Concentration (ppb) | |
|---|---|---|---|---|
| Treatment Number | Days Carbadox Withdrawn | No. of Animals | Liver | Muscle |
| T2 | 14 | 5 | 51.93 ± 15.14 | <LOQ* |
| T3 | 21 | 5 | 29.09 ± 8.20 | <LOQ |
| T4 | 28 | 5 | 17.72 ± 4.72 | <LOQ |
| T5 | 35 | 5 | 11.23 ± 1.86 | <LOQ |
| T6 | 42 | 3 | 11.16 ± 2.13 | <LOQ |
| T7 | 49 | 1 | 10.90 ± 2.35 | <LOQ |

*$LOQ_{liver,\ muscle}$ = 5 ppb
$LOD_{liver,\ muscle}$ = 2 ppb

**7.** Withdrawal period determination: A tolerance of 30 ppb was previously established for QCA (the marker residue) in swine liver (the target tissue). The withdrawal period was based on a statistical analysis of the depletion data, using an upper tolerance limit containing 99 percent of the population with a 95 percent confidence limit. Using the uncorrected residue data for liver from Days 14 to 49, a withdrawal period of 39.34 days was calculated. Based on this data, a 42-day withdrawal period was assigned for the use of MECADOX® 10 in swine.

E. Regulatory method

Residues of quinoxaline-2-carboxylic acid are determined using a gas chromatographic assay with electron capture detection. The method has a limit of quantification of 5 ppb. The method is on display in the Dockets Management Branch (HFA-305), Room 1061,5630 Fishers Lane, Rockville, Maryland 20852.

## VII. AGENCY CONCLUSIONS

A tolerance of 30 ppb was previously established for QCA (the marker residue) in swine liver (the target tissue). With this supplemental NADA, a pre-slaughter withdrawal period of 42 days was assigned for the use of MECADOX® 10 (carbadox) Type A Medicated Article in swine feed. The withdrawal period was based on a statistical analysis of the depletion data, using an upper tolerance limit containing 99 percent of the population with a 95 percent confidence limit. The LIMITATIONS section in 21 CFR 558.115 will be amended to reflect the 42-day withdrawal period.

In accordance with 21 CFR 514. 10f, this is a Category 11 supplement. The approval of this change required a reevaluation of the slaughter withdrawal period according to current food safety guidance. Accordingly, this approval did not require a reevaluation of target animal safety or effectiveness data in the parent application.

The agency has determined under 21 CFR 25.33(a)(1) that this action is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

MECADOX® 10 is not currently under any unexpired U.S. patents.

## VIII. APPROVED PRODUCT LABELING (Attached)

A copy of the facsimile labeling is attached to this document:

A. Facsimile Bag Label - MECADOX® 10 Type A Medicated Article

B. Specimen (Bluebird) Type B Feed Medicated Feed

C. Specimen (Bluebird) Type C Feed Medicated Feed

FRONT

GUSSET

OPEN
PULL NARROW TAPE

# Mecadox® 10
*(carbadox)*

## *Type A Medicated Article*

**Active Drug ingredient:**
*Carbadox*..... 2.2% *(10 g/lb)*

**Indications for Use**
Control of swine dysentery (vibrionic dysentery, bloody scours or hemorrhagic dysentery); control of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis*); increased rate of weight gain and improved feed efficiency in swine,

**WARNING: For use in the manufacture of complete swine feeds and/or swine protein supplement feeds only.**

**CAUTION:** Certain components of animal feeds, including medicated premixes, possess properties that may be a potential health hazard or a source of personal discomfort to certain individuals who are exposed to them. Human exposura should, therefore, be minimized by observing the general industry standards for occupational health and safety.
Precautions such as the following should be considered: dust masks or respirators and protective clothing should be worn; dust-arresting equipment and adequate ventilation should be utilized; personal hygiene should be observed; wash before eating or leaving a work site; be alert for signs of allergic reactions—seek prompt medical treatment if such reactions are suspected.

**SEE BACK PANEL FOR FURTHER USE DIRECTIONS**

**STORE IN A DRY, COOL PLACE**

## *Net Weight 40 lb (18.2 kg)*

NADA #41-061, Approved by FDA
989
99-7292-W-6

Pfizer

V1000-04H 7911-00

Mecadox® 10
*(carbadox)*

BACK

GUSSET

01100872193100043001

# Mecadox® 10
*(carbadox)*

## *Type A Medicated Article*

TAKE TIME
OBSERVE LABEL DIRECTIONS

**COMPLETE SWINE FEED**
**Mixing and Use Directions**

| Indications for Use | Amount of Drug | lb of Mecadox 10/ton of Complete Feed |
|---|---|---|
| Increased rate of weight gain and improved feed efficiency | 0001 1-0.00275% (10 –25 g/ton) | 1 f)–2.5 lb |
| Control of swine dysentery (vibrionic dysentery, bloody scours or hemorrhagic dysentery); control of bacterial swine enteritis (salmonellosis *or necrotic* enteritis caused by Salmonella *choleraesuis*); increased rate of weight gain and improved feed efficiency. | *0* 0055% (50 g/ton) | 501b |

**PROTEIN SUPPLEMENT**
**Mixing and Use Directions**

| Amount of Supplement per Ton of Complete Feed (lb) | lb of Mecadox 10 per Ton of Protein Supplement | | |
|---|---|---|---|
| | Desired Level of Mecadox in Complete Feed | | |
| | 0.0055% f50 g/ton) | 0.00275% (25 g/ton) | 0.001 f% (10 11.bald |
| 1000 | *10* | 5 | 2 |
| 667 | 15 | 7 | 3 |
| 500 | 20 | 10 | 4 |
| 250 | 40 | *20* | 8 |
| *100* | 100 | *50* | *20* |
| *75* | *133* | *67* | *27* |
| *50* | *200* | 100 | *40* |
| *40* | 250 | *125* | 50 |
| *20* | 500 | *250* | 100 |

**WARNING:** Do not feed to swine within 42 days before slaughter.

**CAUTION** Not for use in pregnant swine or swine intended for breeding purposes. Oo not mix in feeds containing bentonite.

U.S. Patent Nos. 3,371,080 and 3,433,871

989
90-7202 -00-6

*Distributed by*
Animal Healt
Exton, PA 19341, USA
Div of Pfizer Inc
NY, NY10017

Mecadox® 10
*(carbadox)*

V1000-04H 7911-00

Placard

BULK

Pig Ration - MX

Type C Medicated Feed

Control of swine dysentery (vibrionic dysentery, bloody scours or hemorrhagic dysentery); control of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis*); increased rate of weight gain and improved feed efficiency in swine when fed in accordance with directions for use.

ACTIVE DRUG INGREDIENT

Carbadox.....0.0055'%0 (50 g/ton)

FEEDING DIRECTIONS

Feed continuously as the sole ration.

Produced in bulk for feeding to swine.
For own use only; not for sale.

CAUTION: Not for use in pregnant swine or swine intended for breeding purposes. Do not mix in feeds containing bentonite.

WARNING: Do not feed to swine within 42 days of slaughter.

Manufactured by
Blue Bird Feed Co.
Blue Bird, MO 00000

(1)

Net Weight _____ Lbs. (Kg)

Pig Ration - MX

Type C Medicated Feed

Control of swine dysentery (vibrionic dysentery, bloody scours or hemorrhagic dysentery); control of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis*); increased rate of weight gain and improved feed efficiency in swine when fed in accordance with directions for use.

ACTIVE DRUG INGREDIENT

| | |
|---|---|
| Carbadox | 0.0055% (50 g/ton) |

GUARANTEED ANALYSIS

| | |
|---|---|
| Crude Protein (Min) | XX.XX% |
| Lysine (Min) | XX.XX% |
| Crude Fat (Min) | XX.XX% |
| Crude Fiber (Max) | XX.XX% |
| Calcium (Min) | XX.XX% |
| Calcium (Max) | XX.XX% |
| Phosphorus (Min) | XX.XX% |
| Salt (Min) | XX.XX% |
| Salt (Max) | XX.XX% |
| Selenium (Min) | XX ppm |
| Zinc(Min) | XX ppm |

INGREDIENTS
(Ingredients as defined by AAFCO.)

FEEDING DIRECTIONS
Feed continuously as the sole ration.

Produced in bulk for feeding to swine.
For own use only; not for sale.

CAUTION: Not for use in pregnant swine or swine intended for breeding purposes. Do not mix in feeds containing bentonite.

WARNING: Do not feed to swine within 42 days of slaughter,

Manufactured by
Blue Bird Feed Co.
Blue Bird, MO 00000

Net Weight _____Lbs. (Kg)

Swine Ration Supplement - MX

Type B Medicated Feed

Control of swine dysentery (vibrionic dysentery, bloody scours or hemorrhagic dysentery); control of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis*); increased rate of weight gain and improved feed efficiency in swine when fed in accordance with directions for use.

ACTIVE DRUG INGREDIENT

| | |
|---|---|
| Carbadox | 0.55-0.01 1% (5000 -100 g/ton) |

GUARANTEED ANALYSIS

| | |
|---|---|
| Crude Protein (Min) | XX.XX% |
| Lysine (Min) | XX.XX% |
| Crude Fat (Min) | XX.XX% |
| Crude Fiber (Max) | XX.XX% |
| Calcium (Min) | XX.XX% |
| Calcium (Max) | XX.XX% |
| Phosphorus (Min) | XX.XX% |
| Salt (Min) | XX.XX% |
| Salt (Max) | XX.XX% |
| Selenium (Min) | XX ppm |
| Zinc(Min) | XX ppm |

INGREDIENTS
(Ingredients as defined by AAFCO.)

MIXING DIRECTIONS [*Note: Grind pellets before or during mixing.]*

Mix 20 – 1000 lbs. of this feed to make one ton of complete feed to provide 50 g/ton carbadox for control of swine dysentery (vibrionic dysentery, bloody scours or hemorrhagic dysentery); control of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis*); increased rate of weight gain and improved feed efficiency, fed at a level of 0.0055% (50 g/ton).

FEEDING DIRECTIONS

Do not feed undiluted. Complete feeds are to be fed continuously as the sole ration.

CAUTION: Not for use in pregnant swine or swine intended for breeding purposes. Do not mix in feeds containing bentonite.

WARNING: Do not feed to swine within 42 days of slaughter.

Manufactured by
Blue Bird Feed Co.
Blue Bird, MO 00000

(3)

Placard

BULK

Pig Ration - MX

Type C Medicated Feed

Increased rate of weight gain and improved feed efficiency in swine when fed in accordance with directions for use.

ACTIVE DRUG INGREDIENT

Carbadox.....0.0011- 0.00275% (10 -25 g/ton)

FEEDING DIRECTIONS:

Feed continuously as the sole ration.

Produced in bulk for feeding to swine.
For own use only; not for sale.

CAUTION: Not for use in pregnant swine or swine intended for breeding purposes. Do not mix in feeds containing bentonite

WARNING: Do not feed to swine within 42 days of slaughter.

Manufactured by
Blue Bird Feed Co.
Blue Bird, MO 00000

Net Weight _____Lbs. (Kg)

Pig Ration - MX

Type C Medicated Feed

Increased rate of weight gain and improved feed efficiency in swine when fed in accordance with directions for use.

ACTIVE DRUG INGREDIENT

| | |
|---|---|
| Carbadox | 0.0011- 0.00275% (10 -25 g/ton) |

GUARANTEED ANALYSIS

| | |
|---|---|
| Crude Protein (Min) | XX.XX% |
| Lysine (Min) | XX.XX% |
| Crude Fat (Min) | XX.XX% |
| Crude Fiber (Max) | XX.XX% |
| Calcium (Min) | XX.XX% |
| Calcium (Max) | XX.XX% |
| Phosphorus (Min) | Xx.x.x% |
| Salt (Min) | XX.XX% |
| salt (Max) | XX.XX% |
| Selenium (Min) | XX ppm |
| Zinc(Min) | XX ppm |

INGREDIENTS

(Ingredients as defined by AAFCO.)

FEEDING DIRECTIONS

Feed continuously as the sole ration.

CAUTION: Not for use in pregnant swine or swine intended for breeding purposes. Do not mix in feeds containing bentonite.

WARNING: Do not feed to swine within 42 days of slaughter.

Manufactured by
Blue Bird Feed Co.
Blue Bird, MO 00000

Net Weight _____ Lbs.

Swine Ration Supplement - MX

Type B Medicated Feed

ACTIVE DRUG INGREDIENT

Carbadox ..... 0.11 - 0.275% (1000 -2500 g/ton)

GUARANTEED ANALYSIS

| | |
|---|---|
| Crude Protein (Min) | XX.XX% |
| Lysine (Min) | XX.XX% |
| Crude Fat (Min) | XX.XX% |
| Crude Fiber (Max) | XX.XX% |
| Calcium (Min) | XX.XX% |
| Calcium (Max) | XX.XX% |
| Phosphorus (Min) | XX.XX% |
| salt (Min) | XX.XX% |
| Salt (Max) | XX.XX% |
| Selenium (Min) | XX ppm |
| Zinc(Min) | XX ppm |

INGREDIENTS

(Ingredients as defined by AAFCO.)

MIXING DIRECTIONS: [NOTE: *Grind pellets before or during mixing.]*

Mix 40-100 lbs. of this feed to make one ton of complete feed to provide 50 g/ton carbadox for control of swine dysentery (vibrionic dysentery, bloody scours or hemorrhagic dysentery); control of bacterial swine enteritis (salmonellosis or necrotic enteritis caused by *Salmonella choleraesuis*); increased rate of weight gain and improved feed efficiency, fed at a level of 0.0055% (50 g/ton).

Mix 8-20 lbs. of this feed to make one ton of complete feed to provide 10-25 g/ton carbadox for increased rate of weight gain and improved feed efficiency in swine when fed in accordance with directions for use, fed at a level of 0.0011 -0.00275% (10 -25 g/ton). Feed continuously as the sole ration.

FEEDING DIRECTIONS

Do not feed undiluted. Complete feeds are to be fed continuously as the sole ration.

CAUTION: Not for use in pregnant swine or swine intended for breeding purposes. Do not mix in feeds containing bentonite.

WARNING: Do not feed to swine within 42 days of slaughter.

Manufactured by
Blue Bird Feed Co.
Blue Bird, MO 00000